Pyridine alcohols and thiols

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CHAPTER 4

Complexation of Pyridine Alcohols and Thiols.*

Abstract: Complexes of the pyridine diols **2.1** and dithiols **3.1** with protic acids as well as zinc salt were investigated. HCl complexes were formed with pyridine dithiol **3.1b**, pyridine diols **2.1d** and **2.7b**. The complex **3.1b**·HCl lost HCl from the solid under reduced pressure. This remarkable physical property suggests complexation of covalent HCl. On the other hand X-ray diffraction, ^{1}H NMR data and IR spectroscopy all point, however, to an ionic character of the HCl bond. Complexes of diol **2.1b** and thiols **3.1b** and **3.11f** with HBr were also prepared. Addition of the HCl and HBr complexes to cyclohexene oxide **4.1a** or cyclopentene oxide **4.1b** afforded the corresponding chloro- and bromohydrins. No reproducible enantioselection was observed when chiral complexes were used. Complexation of HNO_3 with pyridine diol **2.1b** afforded the acid complex. With pyridine dithiol **3.1b** a complex with HNO_3 could be prepared at 0 °C. Complex formation at room temperature gave rise to oxidation of the thiol groups. Zinc complexes of the pyridine diols **2.1** were easily prepared. Complexation of pyridine dithiol **3.1b** with $Zn(NO_3)_2$ gave the dimeric zinc complex **4.4b**. Complexation with $ZnCl_2$ gave rise to 28% of the dimeric zinc complex **4.4b** and for 60% a complex of HCL·$ZnCl_2$·ROH with dithiol **3.1b** was obtained as established by X-ray diffraction. Complexation of **3.1f** with $Zn(NO_3)_2$ afforded the monomeric zinc complex **4.5f**.

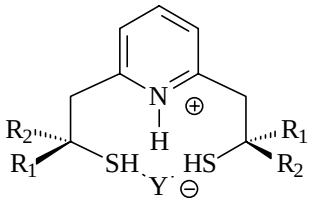
4.1 Introduction.

Previous research on pyridine diol **2.1b** revealed a high affinity of this tridentate ligand for the complexation of HCl.[1] It was found that the host organizes itself so that the acid is perfectly enclosed in a cavity wherein Cl is hydrogen bonded to the two hydroxyl groups and the proton of HCl is directed towards the pyridine nitrogen. In order to investigate the affinity of the pyridine diols **2.1** and dithiols **3.1** for acids and to study the self-organization of the cavity of these molecules various complexes of these ligands were prepared and studied with X-ray diffraction.

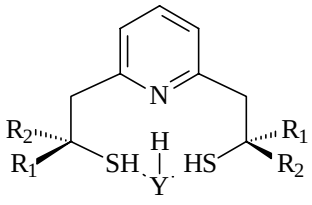
4.2 Complexes with Acids.

4.2.1 Complexation of HCl.

To obtain complex **3.1b**·HCl the tridentate pyridine dithiol **3.1b** was allowed to react with one equivalent of HCl using a freshly prepared titrated solution of HCl in chloroform. It is also possible to use HCl gas in excess for the complex formation, although a complication is slow elimination of H_2S affording the mono and di-olefins as indicated by ^{1}H NMR. The ^{1}H NMR of the complex **3.1b**·HCl shows remarkable differences compared to the free ligand **3.1b** indicating substantial differences in solution. A downfield shift of the signal from the benzylic protons (0.66 ppm) and increased complexity of the signals from the protons of the adamantyl moiety compared to the free ligand are observed. Also a large downfield shift of the pyridine protons is observed (0.62 ppm for 4-hydrogen and 0.29 ppm for 3- and 5-hydrogen) indicating that protonation of the nitrogen has taken place. This seems to be a general indication of protonation of pyridine diols and dithiols.



Formulation A



Formulation B

The large chemical shifts of the pyridine protons in the ^{1}H NMR on complexation of HCl are consistent with a complex that consists of a tight ion pair (formulation A) rather than covalent HCl (formulation B). However, upon drying of the HCl-complex under high vacuum at room temperature we observed that HCl evaporates from the complex and free ligand **3.1b** is obtained. This is not observed for other complexes, for example 2,6-lutidine·HCl. This physical property would be consistent with a covalent HCl (formulation B). IR spectra of

3.1b·HCl in KBr are complicated by the fact that the HCl absorptions are hidden under the strong adamantyl C-H bands. This led us to the study of the DCl complex. In some cases the **3.1b**.DCl complex shows a sharp absorption at 2211 cm^{-1}, which is partially masked by a broad pyridine-D^+ absorption in the region 2212 to 1850 cm^{-1}. The 2211 cm^{-1} absorption is close to that expected for *covalent* D-Cl. For example, values of 2091 cm^{-1} and 2090 cm^{-1} for monomeric DCl in, respectively, the gas phase[2] and in an Ar matrix[3] are given in the recent literature. The ^{1}H NMR spectra as well as the infrared spectra indicate clearly that D-Cl has not exchanged with S-H (attempts to prepare the S-D derivative of **3.1b** have been unsuccessful owing to the failure of the S-H groups to exchange with D at a measurable rate either in free **3.1b** under neutral conditions or in the D-Cl complex). The 2211 cm^{-1} absorption is not observed in the D-Cl complex with 2,6-lutidine.

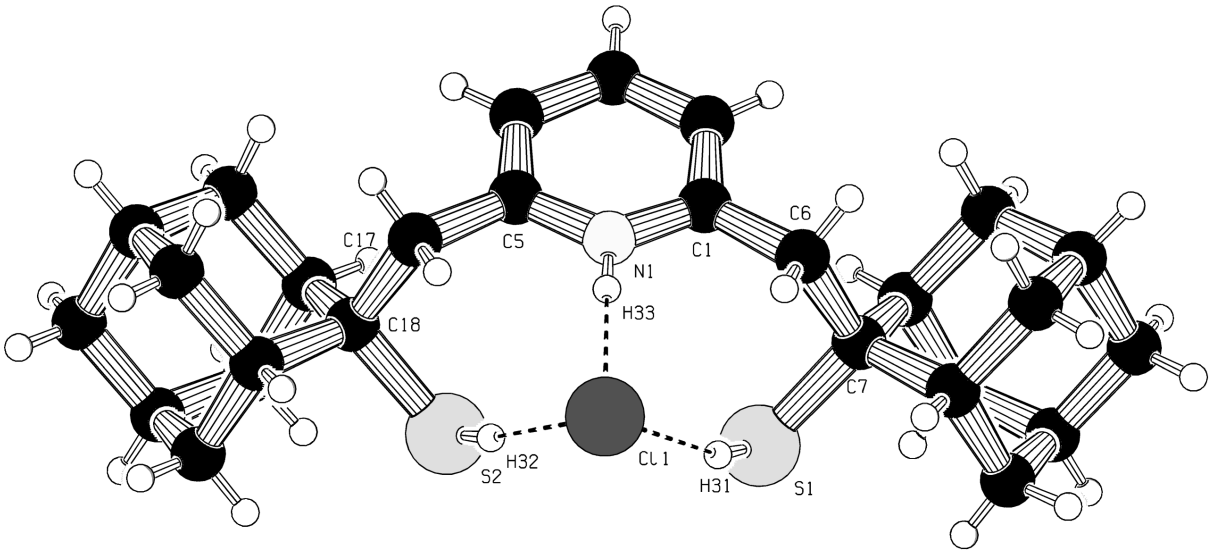


Figure 4.1 *Crystal structure of **3.1b**·HCl.*

More information of this complex was obtained from the crystal structure of the complex **3.1b**·HCl (Figure 4.1). Monomeric HCl is firmly embedded in a cavity and held in place by bonding to the pyridine nitrogen and the two thiols. The free pyridine dithiol **3.1b** (see Figure 3.1) is not preorganized in this arrangement. In the complex the thiol groups are clearly hydrogen bonded to the chloride although the bonds are unequal [H(31)...Cl(1) 2.58(3) Å; H(32)...Cl(1) 2.45(5) Å] likely the result of crystal packing effects, since in the ^{1}H NMR no differences can be found between the benzylic protons. The thiol groups bind from the same face (roughly a plane of symmetry in the complex).[3a] The H...Cl bond distance in **3.1b**·HCl is 2.19 Å, which is 0.92 Å longer than the covalent HCl bond length in the gas phase (1.27 Å).[4] A search of the Cambridge Data Base for pyridine...HCl complexes revealed an average bond length for the H...Cl bond distances of 2.20 Å with a deviation of 0.17 Å for 39 hits. For this screening a minimum N..H..Cl bond angle of 120° was included. Based on

these data and our experimental data we conclude that the HCl complex has an ionic character. However, the physical characterization of the complex suggest that transition to a more weakly bound form involving covalent HCl might be relatively easy.

The HCl complex of pyridine diol **2.1e** was prepared by passing through an excess of HCl. No elimination of water was observed. In the ^{1}H NMR spectrum large downfield chemical shifts for the pyridine protons were observed (0.55 ppm for the 4-hydrogen; 0.39 ppm for the 3- and 5-hydrogen), indicating a protonation of the nitrogen. Downfield shifts for the benzylic protons (0.38 ppm) were also observed. Furthermore they gave rise to a set of four signals all belonging to the same CH_2 groups the protons of which have now become nonequivalent. Probably due to the limited rotation on the NMR time scale the benzylic protons of **2.1e**·HCl have become diastereotopic. Apparently the structure of the complex has a locked conformation on the NMR time scale, whereas the free ligand **2.1e** has free rotation. X-ray analysis of the complex **2.1e**·HCl in comparison with the X-ray analysis of the free ligand **2.1e** (see Figure 2.2) revealed some remarkable differences. The molecular structure of **2.1e** shows an open C_2-symmetrical conformation of the ligand. The nitrogen forms strong intramolecular hydrogen bonds with the hydroxyl groups of the camphor moiety (H(61)…N(1) = 2.02(4), O(1)…H(61) = 0.84(4), H(62)…N(1) = 2.11(4), O(2)…H(62) = 0.79(4) Å) and is in this arrangement preorganized for complexation. In the X-ray analysis of **2.1b** only one of the hydroxyl groups forms a H-bond with the nitrogen of the pyridine ring and the other hydroxyl group forms a H-bond with the first hydroxyl group.[5]

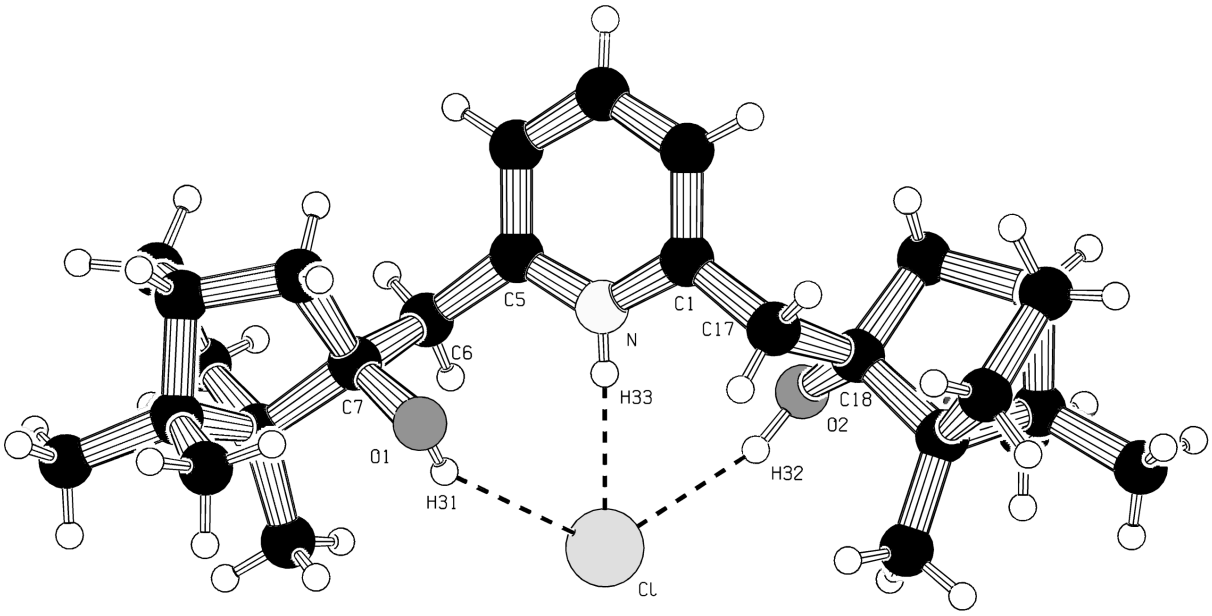


Figure 4.2 *Crystal structure of **2.1e**·HCl.*

The X-ray structure of complex **2.1e**·HCl (Figure 4.2) shows that the hydrogen chloride is firmly embedded in a cavity and held in place by bonding to the pyridine nitrogen and to the

hydroxyl groups. The hydroxyl groups are clearly hydrogen bonded to the chloride (H(31)…Cl(1) = 0.79(4), H(32)…Cl(1) = 0.97(4) Å). The bonds though are not of an equal length which is probably a result of the crystal packing effects. The pyridine nitrogen forms a strong bond with the hydrogen of acid (N(1)…H(33) = 0.85(4) Å) and the distance between the chloride and the hydrogen suggests an ionic character of the encapsulated acid (Cl(1)…H(33) = 2.23(4) Å).

Complexation of HCl with the C_s-symmetrical pyridine diol **2.7b** was also found to be possible. Again large downfield shifts for the pyridine protons are observed. Whether both hydroxyl groups of the ligand **2.7b** are involved in the binding of the HCl cannot be concluded from the spectral data. X-ray analysis of this complex, however, gave satisfactory evidence that only one hydroxyl group is involved (Figure 4.3). The crystal consisted of two independent asymmetric units, which each contains two anions, two chloride cations and one solvent dichloromethane molecule. Both units show hydrogen bonding between the chloride anion and one of the hydroxyl groups (O(2)-H(102)…Cl(3) = 2.18(3) Å) and the proton at the pyridine nitrogen (N(1)-H(111)…Cl(3) = 2.36(3) Å for unit 1, and O(3)-H(103)…Cl(4) = 2.27(3) Å, N(2)-H(112)…Cl(4) = 2.38(3) Å for unit 2). The hydroxyl group that does not form a hydrogen bond with the chloride is hydrogen bonded to the other hydroxyl group of the same molecule (O(1)…H(102) 2.03(4) Å for unit 1 and O(3)…H(104) 1.94(4) Å for unit 2). Although the HCl complex of **3.11f** (Figure 3.3) consists of a polymeric strain this HCl complex is monomeric.

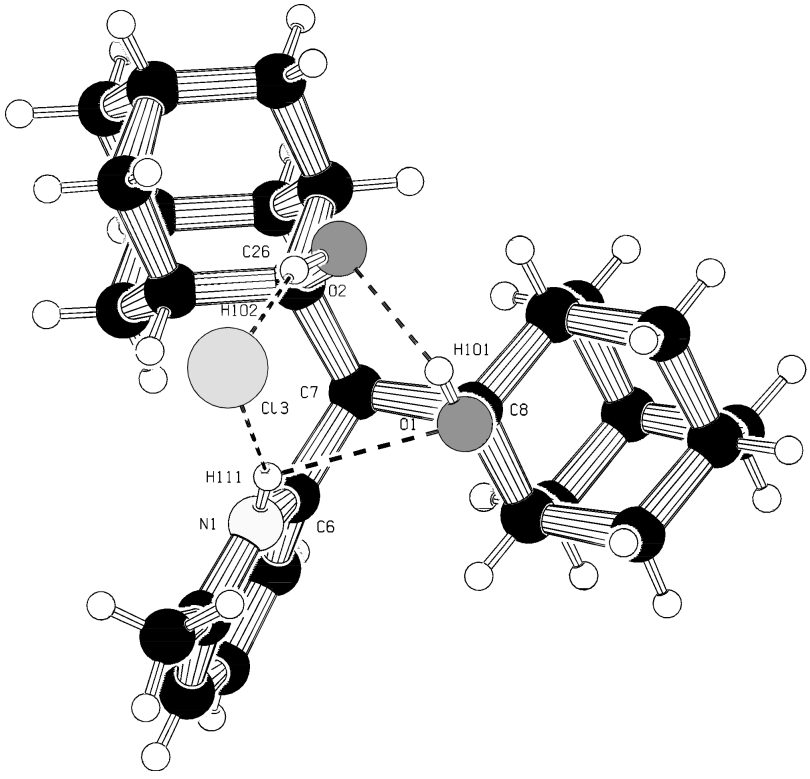


Figure 4.3 *Crystal structure of unit 1 of **2.7b**·HCl.*

4.2.2 Complexation of HBr and Nitric Acid.

Beside the complexation of HCl with these ligands the complexation of HBr was also possible. Complexes of **2.1b**, **3.11f**, and **3.1b** were prepared by slowly passing HBr through a solution of the free ligand in chloroform at 0°C. ^{1}H NMR of all complexes showed the protonation of the pyridine nitrogen. Again downfield shifts for the benzylic protons were observed. The ^{1}H NMR of **3.11f**·HCl, furthermore, shows a set of 4 signals for the benzylic protons indicating a locked conformation on NMR scale as was also seen for the HCl complex of **3.11f**.

Complexation of HNO_3 was also found to be successful. The complex of HNO_3 with pyridine diol **2.1b** was prepared by adding a HNO_3 solution (57%) to a solution of the free ligand. The product could be isolated after concentration and recrystallization from methanol. The HNO_3 complex of pyridine thiol **3.1b** was more troublesome due to the fact that the thiol groups are partly oxidized by the HNO_3 at ambient temperature. Complexation at 0°C, however, afforded the **3.1b**·HNO_3 complex. Suitable crystals for X-ray diffraction of the complex **3.1b**·HNO_3 could be obtained from chloroform/hexane (Figure 4.4).

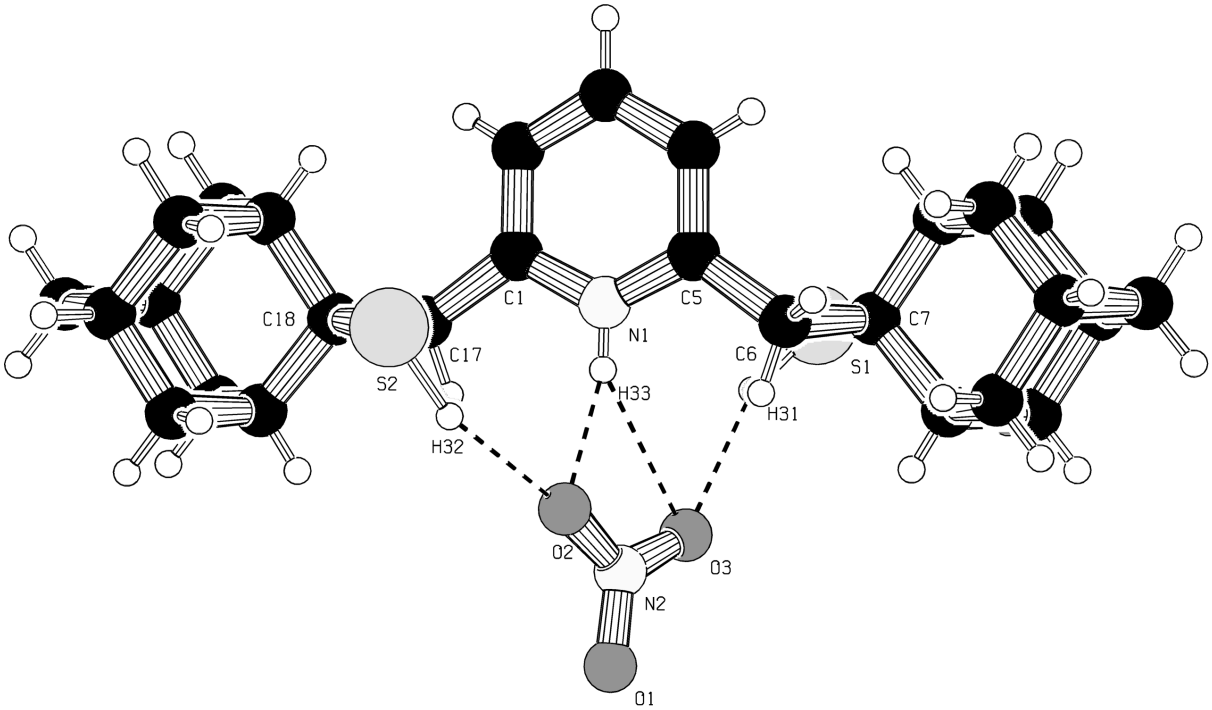
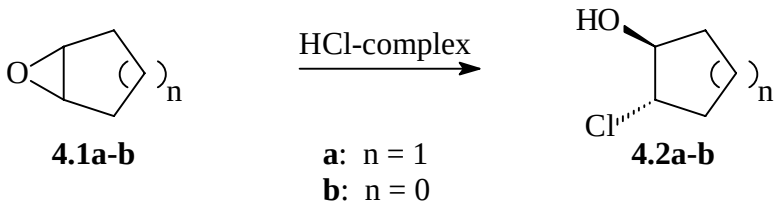


Figure 4.4 *Crystal structure of **3.1b**·HNO_3.*

There is a noteworthy difference between **3.1b**·HCl and **3.1b**·HNO_3. First of all the cavity that is formed for the complexation of HNO_3 is bigger than in the HCl complex. The flexibility of the ligand allows the adjustment of the cavity when larger acids coordinate. The proton H(33) at the pyridine nitrogen forms a strong bond with O(2) (1.92(5) Å) whereas the bond between H(33) and O(3) is longer (2.58(5) Å). Both thiol groups are hydrogen bonded to the oxygens of the acid (H(32)…(O2) 2.26(5) Å and H(31)…O(3) 2.21(5) Å).

4.3 Hydrochlorination of Epoxides Using HCl-complexes.

Addition of HCl to strained heterocyclic rings such as those of epoxides is known from the literature although the reaction is not extensively applied, likely because of the lack of suitable methods to generate mild reaction conditions to perform the ring opening reaction. Addition of hydrogen chloride to a reaction mixture gives an acidic medium which can lead to unwanted side reactions such as epimerization. It is also difficult to control the quantity of hydrogen chloride added. We observed that upon addition of the hydrogen chloride complex **2.1b**·HCl to cyclohexene oxide **4.1a** or cyclopentene oxide **4.1b**, the epoxide is opened though nucleophilic attack of the chloride forming the corresponding epichlorohydrin quantitatively (Scheme 4.1).



4.1a-b **a**: n = 1 **b**: n = 0 **4.2a-b**

Scheme 4.1 *Ring opening of epoxides with hydrogen chloride complexes.*

Although the hydrogen chloride is encapsulated within the molecular structure of the ligand it is apparently not so tightly bond that it cannot react with the epoxide. Ring opening provides the *trans* product selectively within 3 hour as deducted form ^{1}H NMR. No traces of isomerization to the *cis* product is observed. Using the hydrogen chloride complexes mild conditions for ring opening are generated and just one equivalent of hydrogen chloride is added preventing unwanted side reactions. Using 2,6-lutidine·HCl ringopening can also be effectuated, giving a cheap alternative for this reaction.

Ring opening of prochiral cyclohexene oxide and cyclopentene oxide making use of chiral hydrogen chloride complexes like **2.1d**·HCl and **3.11f**·HCl was investigated. When epoxides **4.1a** and **4.1b** were stirred with complexes **2.1d**·HCl and **3.11f**·HCl selective ring opening to the *trans* epichlorohydrins **4.2a** and **4.2b** occurred. Determination of the enantiomeric excess,[6] however, gave only low (0-10%) and unreproducible selectivities. The steric aspects of the ligand seem to have only a minor influence on the approach of the epoxide to the chloride. Thus far no reproducible enantioselective addition has been observed.

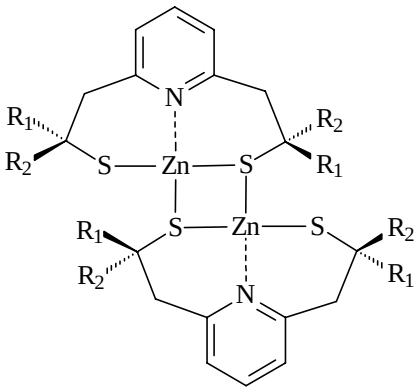
Ring opening of the epoxides with the hydrogen bromide complexes **2.1b**·HBr, **3.1f**·HBr, and **3.11f**·HBr gave rise to the *trans* epibromohydrins **4.3a** and **4.3b**. Again low and unreproducible enantioselectivities with the chiral hydrogen bromide complexes were observed.

4.5 Complexes with Zinc.

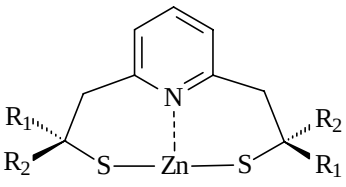
Encapsulation of various metals like Zn[7], Ti,[8] Mo,[9] Os,[10] Zr,[11] and Ru[12] have been reported for **2.1a, 2.1b** and **3.1a**. Molybdenum complexes of both the diol **2.1a** and the dithiol **3.1a** are known as models for molybdenum enzymes.[9] The zinc complexes of pyridine diol **2.1b** and dithiol **3.1a** are of interest as models for the catalytic active zinc at the active site of Horse Liver Alcohol Dehydrogenase (HLADH) although catalytic activity with these complexes is low.[7] In order to examine more closely the complexation abilities of the pyridine alcohols and thiols with zinc various complexes were synthesized.

When pyridine diol **2.1b** was stirred with $Zn(NO_3)_2$ overnight the complex was formed. ^{1}H NMR shows a downfield shift for the pyridine protons indicating that the pyridine ring is involved in the complexation of the zinc. These results are in accordance with the result reported for the complexes of pyridine diols **2.1c** and **2.1d** with $Zn(NO_3)_2$. A chiral zinc complex was obtained by reaction of **2.1e** with $Zn(NO_3)_2$. A relatively large chemical shift for the pyridine protons in the ^{1}H NMR was observed (0.5 ppm for the 3- and 5-hydrogens and 0.6 ppm for the 4-hydrogen). Furthermore the benzylic protons give rise to a AB-system caused by the locked conformation of the complex. The ^{1}H NMR spectrum also indicates an impact on the camphor moiety: the methyl groups are shifted downfield whereas the other alkyl groups are shifted upfield. Complexation of zinc seems to have a great impact on the whole structure of the molecule. When **2.1e** was allowed to form a complex with $Zn(ClO_4)_2$ a similar complex was formed. However, the impact of coordination of this zinc reagent has far less influence on the camphor moiety and only upfield shifts for the alkyl groups are observed. Complexation of $Zn(NO_3)_2$ with the C_s-symmetrical pyridine diol **2.7b** afforded colorless crystals. For this complex also large chemical shifts of the pyridine protons are observed indicating that the complex is formed. Furthermore large downfield shifts for the benzylic proton as well as the methyl group are observed. The signals for the adamantyl moiety becomes extremely complicated on complexation.

Zinc complexes with pyridine dithiols **3.1** have been reported previously.[7] Zinc complexes of **3.1a** and **3.1c** were found to give dimeric complexes **4.4**, whereas, the zinc complex of **3.1d** owing to the large fluorenyl groups gave monomeric zinc complex **4.5**. We have assumed that for these complexes to act as a model for the enzyme HLADH they must be monomeric otherwise the zinc atom is coordinatively saturated and unable to act as a catalyst.



4.4a-c



4.5d,f

a: R_1,R_2 = phenyl
b: R_1,R_2 = adamantyl
c: R_1,R_2 = methyl
d: R_1,R_2 = fluorenyl
f: R_1,R_2 = fenchyl

Since the allylic moieties of pyridine dithiols **3.1b** and **3.1f** are bulky complexation of zinc could afford monomeric complexes. When dithiol **3.1b** was stirred with $Zn(NO_3)_2$ a poorly soluble dimeric zinc complex **4.4b** precipitated as a white solid as was observed in the ^{1}H NMR. Since all benzylic protons are nonequivalent these protons give rise to a set of eight signals. Apparently the adamantyl moiety does not shield the zinc enough to prevent dimerization. When pyridine dithiol **3.1b** was allowed to complex with $ZnCl_2$ in methanol again the dimeric zinc complex **4.4b** precipitated. Removal of the solvent afforded a second product. The ^{1}H NMR of this product shows extremely large downfield shifts of the pyridine protons (1.19 ppm for the 4-hydrogen and 0.54 ppm for the 3- and 5-hydrogens). Furthermore methanol is still present in the product. Evaporation of methanol under high vacuum afforded a solid that was insoluble in chloroform. Addition of ethanol led to dissolution of the solid indicating that alcohol is embedded in the complex. Although the chemical shifts of 1.19 ppm for the 4-hydrogen and 0.54 ppm for the 3- and 5-hydrogen are very large for a zinc complex qualitative analysis revealed the presence of zinc. Crystals Suitable for X-ray diffraction were grown from chloroform/hexane (Figure 4.5).

X-ray crystallographic structure determination reveals the structure to be dimeric complex **4.6** in which HCl is encapsulated, although in an unusual manner, in the cavity of the pyridine dithiol. The Cl from the HCl is strongly coordinated to an equivalent of $ZnCl_2$ (Cl(2)…Zn 2.2425(8) Å). The fourth coordination place of this $ZnCl_2$ is filled with a methanol or ethanol molecule. The initial reaction took place in methanol, after removal of a part of the methanol and upon addition of ethanol the fourth coordination position is filled with methanol as well as ethanol in a ratio of 56:44. The hydroxyl groups of the alcohols are hydrogen bonded to the chloride atom of the other part of the dimer (2.32(3) Å). These two hydrogen bonds keep the entire structure together. Remarkable in this complex is the binding of the hydrogen chloride by the thiol groups in a *trans* fashion. In the complex of **3.1b**·HCl the HCl is bonded in a *cis* fashion. The coordination is likely due to influences of the zinc chloride on the crystal packing.
The mechanism of formation of this complex is probably as follows. Initially addition of $ZnCl_2$ to the free ligand **3.1b** led to the formation of the monomeric zinc complex upon which two

equivalents of HCl are released. This monomeric complex is unstable and associates to the dimer **4.4b**. The released HCl is encapsulated by free ligand and this complex forms a stable bond with $ZnCl_2$ still present in the mixture. After 1/3 of the ligand has formed the dimeric zinc **4.4b** complex the remaining 2/3 of the ligands is converted to the HCl complex.

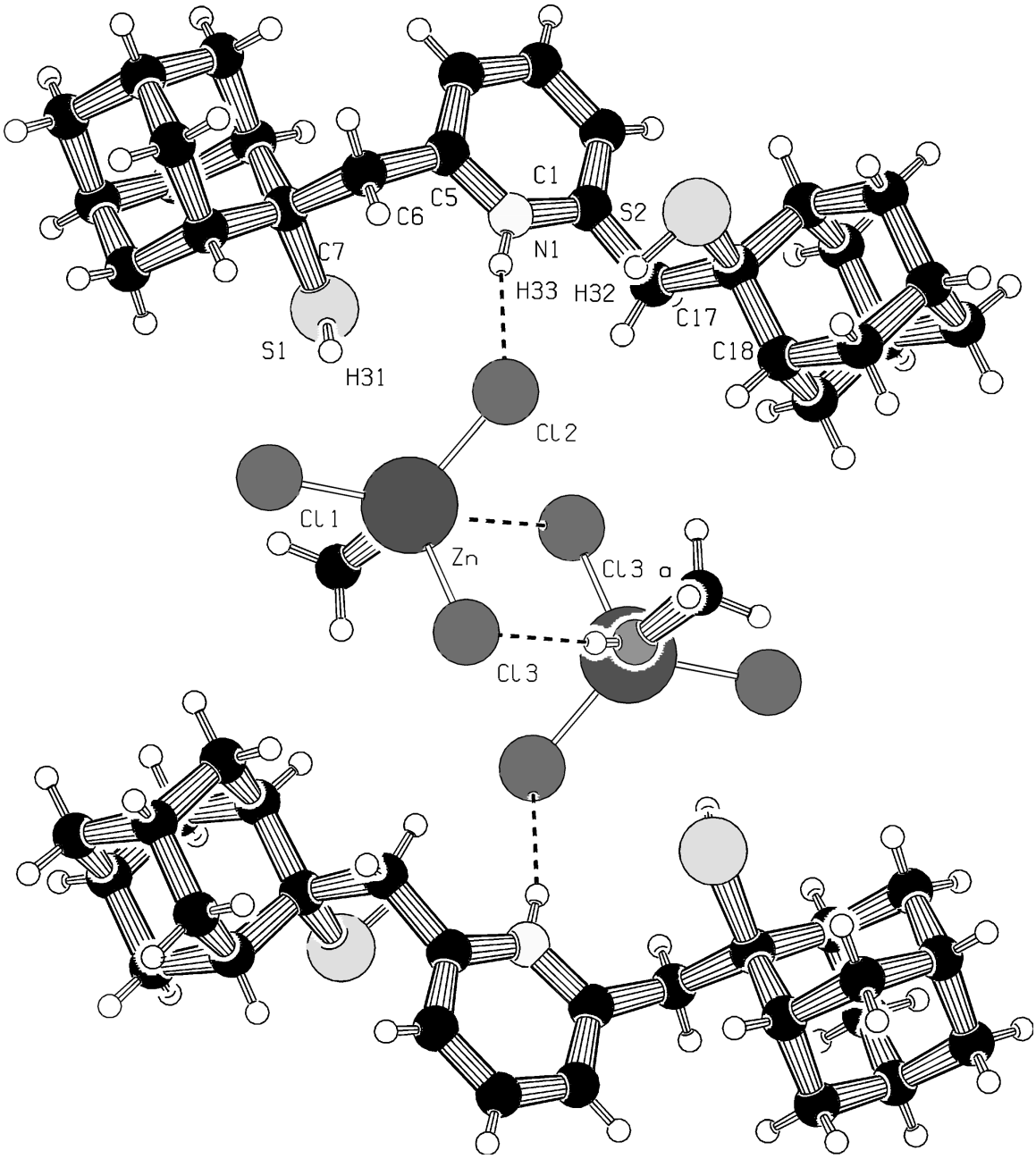


Figure 4.5 *Crystal structure of **4.6.***

When chiral pyridine dithiol **3.1f** was added to a solution of $Zn(NO_3)_2$ in methanol and stirred for 3 h and after careful removal of the solvent a white solid was obtained. ^{1}H NMR in $CDCl_3$ revealed the monomeric zinc complex **4.5f**. The benzylic protons give rise to only four signals whereas for a dimeric structure eight signals are expected. Mass spectroscopy (electron spray and exact mass) on this complex establishes a monomeric complex. The complex of **3.1f**

with $Co(NO_3)_2$ surprisingly showed a dimeric complex as indicated by ^1H NMR. The monomeric Co complex probably is less stable than the monomeric zinc complex and dimerizes.

4.6 Conclusions.

Complexations of HCl with pyridine diol **2.1e** and with the pyridine thiols **3.11f** and **3.1b** were found to be successful. The complex **3.1b**·HCl showed a remarkable physical property, which point towards complexation of covalent HCl. ^1H NMR data, X-ray diffraction, and infrared spectroscopy of the DCl complex, however, point towards an ionic character of the HCl bond. X-ray diffraction of the C_s-symmetrical pyridine diol **2.7b** complex with HCl revealed that only one of the hydroxyl groups coordinates with the chloride. Complexes with the pyridine diol **2.1b** and thiols **3.1f** and **3.11f** were formed with HBr. Addition of cyclohexene oxide and cyclopentene oxide to these HBr and HCl complexes gave the bromo- and chlorohydrins. When chiral complexes were used low and nonreproducible enantiomeric excesses were obtained. The complexes probably do not shield the acids enough so that enantioselection can occur. Complexes with HNO_3 can also be formed even with the oxidizable dithiol **3.1b** as shown by X-ray analysis. Pyridine diols **2.1b**, **2.1e** and **2.7b** easily give complexes with Zn^{2+}. Complexation of $Zn(NO_3)_2$ with pyridine dithiol **3.1b** gave a dimeric complex **4.4b** whereas complexation with **3.1f** afforded a monomeric complex **4.5f**. When $ZnCl_2$ was used for complexation with **3.1b** some dimeric zinc complex **4.4b** was formed; release of HCl in this reaction gave rise to complexation of the HCl by the ligand and formation of the dimeric HCl·$ZnCl_2$ complex **4.6**. The pyridine diols and dithiols are perfectly capable of complexating metals as well as small acids like HCl, HBr and HNO_3. The size of the cavity in which these substrates bind is flexible and adapts to such a size that the metal or acid perfectly fits the cavity.

4.7 Experimental Section.

General Remarks: See Chapter 2. HCl was prepared from NaCl and H_2SO_4. HBr and DCl were used from lecture bottles. DCl was dried over D_2SO_4.

3.1b·HCl

A solution of dithiol **3.1b** (0.10 g, 0.23 mmol) in 5 mL of $CHCl_3$ under an argon atmosphere was cooled to 0 °C. At this temperature a freshly prepared solution of HCl in chloroform was added. The mixture was stirred for 30 min and after careful evaporation of the solvent at reduced pressure the crude HCl complex was isolated as a white powder, which was crystallized from methanol to afford **3.1b**·HCl as colorless needles (0.11 g., 0.22 mmol, 98%). mp 229-230 °C; ^1H NMR ($CDCl_3$): δ 1.58-1.94 (m, 20H), 2.25 (m, 4H), 2.52 (m, 4H), 3.22 (s, 2H), 4.04 (s, 4H), 7.44 (d, *J* = 8.05 Hz, 2H), 8.11 (dd, *J* = 8.05 Hz, 1H); ^{13}C NMR

($CDC1_3$): δ 27.04 (CH), 27.43 (CH), 33.21 (CH_2), 33.63 (CH_2), 37.77 (CH), 38.99 (CH_2), 42.44(CH_2), 56.16 (C), 124.78 (CH), 142.54 (CH), 155.10 (C); HRMS calcd for $C_{27}H_{38}NS_2$ Cl 475.698, found 439.237 (-HCl)

3.1b.DCl

This product was synthesized according to the HCl analogue **3.1b**·HCl, starting from the dithiol compound **3.1b** (0.13 g, 0.30 mmol) in 5 mL of $CDCl_3$ to which a freshly prepared solution of DCl in $CDCl_3$ was added. Careful evaporation of the solvent yielded the DCl complex as a white powder (0.13 g., 0.28 mmol, 95%). mp 228-230 °C; ^{1}H NMR ($CDCl_3$): δ 1.58-1.94 (m, 20H), 2.25 (m, 4H), 2.52 (m, 4H), 3.22 (s, 2H), 4.04 (s, 4H), 7.44 (d, *J* = 8.05 Hz, 2H), 8.11 (dd, *J* = 8.05 Hz, 1H); ^{13}C NMR ($CDC1_3$): δ 27.0 (CH), 27.4 (CH), 33.2 (CH_2), 33.6 (CH_2), 37.7 (CH), 38.9 (CH_2), 42.5(CH_2), 56.2 (C), 124.7 (CH), 142.5 (CH), 155.1 (C); IR: 3425 (br), 2910 (s), 2860 (s), 2665 (br), 2570 (br), 2480 (br), 2211 (s), 2005 (br), 1630 (s), 1615 (s), 1450 (s), 1100 (s), 920 (s), 735 (s), 720 (s) cm^{-1}.

Crystal Structure of 3.1b·HCl.

Crystal Data: Formula: $[C_{27}H_{38}NS_2]^+.Cl^-.(CH_2Cl_2)$, M = 561.12. Suitable transparent block-shaped crystals of approximate dimensions of 0.17 x 0.41 x 0.05 mm were obtained by recrystallization from dichloromethane. Orthorhombic, P*bcn*, *a* = 15.491(1), *b* = 12.989(1), *c* = 28.081(2) Å, V = 5650.3(7) Å , Z = 8, D = 1.319 g cm , λ(MoK$\bar{\alpha}$) = 0.71073 Å, μ = 4.91 cm, F(000) = 2834, T = 130 K. *Data collection:* The data were collected on an Enraf-Nonius *CAD-4F*^{2} diffractometer (Mo tube, 50 kV, 40 mA, monochromated Mo-K$\bar{\alpha}$ radiation, Δω = 1.05 + 0.34 tg θ), range 8.35° < θ < 18.4°, reflections collected: 7388 independent reflections: 5529. *Solutions and refinement*: The structure was solved by Patterson methods and extension of the model was accomplished by direct methods applied to difference structure factors using the program *DIRDIF*.[13] wR(F^2) = 0.112 for 5529 reflections with $F_o^2 \geq 0$ and R(*F*) = 0.044 for 4507 unique observed reflections with $F_o \geq 4.0\ \sigma(F_o)$ and 477 parameters.

Table 4.1: *Interatomic distances and selected bond angles for compound **3.1b**·HCl*

Interatomic Distances (Å)					
S(1)[a]	-C(7)	1.850(2)[b]	C(17)	-C(18)	1.555(3)
S(2)	-C(18)	1.850(2)	H(31)	-S(1)	1.25(3)
N(1)	-C(1)	1.339(3)	H(32)	-S(2)	1.22(5)
N(1)	-C(5)	1.346(3)	H(33)	-N(1)	0.86(3)
C(1)	-C(6)	1.504(3)	H(31)	-Cl(1)	2.58(3)
C(5)	-C(17)	1.501(3)	H(32)	-Cl(1)	2.45(5)
C(6)	-C(7)	1.554(3)	H(33)	-Cl(1)	2.19(3)

Bond angles (deg.)							
C(1)	-N(1)	-C(5)	124.7(2)	Cl(1)	-H(31)	-S(1)	162(3)
C(1)	-C(6)	-C(7)	116.9(2)	Cl(1)	-H(32)	-S(2)	168(3)
C(5)	-C(17)	-C(18)	116.7(2)	Cl(1)	-H(33)	-N(1)	178(3)
S(2)	-C(18)	-C(17)	107.01(16)	H(31)	-S(1)	-C(7)	97.8(17)
S(1)	-C(7)	-C(6)	107.78(16)	H(32)	-S(2)	-C(18)	97.8(19)
N(1)	-C(1)	-C(6)	118.1(2)	H(33)	-N(1)	-C(1)	118.5(19)
N(1)	-C(5)	-C(17)	118.2(2)	H(33)	-N(1)	-C(5)	116.9(19)

[a] The numbering for the crystal data does not follow the numbering used in nomenclature.

[b] Standard deviation in parentheses.

2.1e·HCl

To a solution of the free ligand **2.1e** (0.20 g, 0.49 mmol) 20 mL in dichloromethane was passed through a slow stream of HCl for 5 min. The mixture was stirred for 1 h and the solvent was evaporated. The solid was recrystallized from water/ethanol (1:2) yielding a colorless solid (0.21g, 0.47 mmol, 95.6 %): mp >200°C; $[\alpha]^{23}_{D}$ +189° (*c* 0.4, chloroform); ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.83 (s,6H), 1.01 (s, 6H), 1.07 (s, 6H), 1.36 (m, 4H), 1.56 (m, 6H), 1.72 (m, 4H), 2.89 (d, *J* = 12.81 Hz, 2H), 3.69 (d, *J* = 12.81 Hz, 2H), 4.18 (s, 2OH), 7.43 (d, *J* = 8.06 Hz, 2H), 8.04 (t, *J* = 8.06 Hz, 1H); ^{13}C NMR (500 MHz, $CDCl_3$): δ 9.58 (q), 20.99 (q), 21.14 (q), 27.13 (t), 30.57 (t), 42.40 (t), 43.88 (t), 44.93 (d), 48.96 (s), 53.37 (s), 80.88 (s), 125.12 (d), 143.7 (d), 155.38 (s). HRMS calcd 447.290; no proper HRMS could be obtained; CI(NH_3) gave a molecular ion at m/e 412 (-HCl). Anal. Calcd for $C_{27}H_{42}NO_2Cl$: C, 72.37; H, 9.45; N, 3.13, Cl 7.91. Found C, 72.21; H, 9.20; N, 3.20, Cl 7.97.

Crystal Structure of 2.1e·HCl

Crystal Data: Formula: $C_{27}H_{42}NO_2^+Cl^-$, M = 448.09, Suitable crystals for an X-ray crystallographic determination were grown from a solution of **2.1e**·HCl in ethanol/water upon slow evaporation of the ethanol. The colorless plate-shaped crystal, used for characterization and data collection, was of approximate size 0.09 x 0.45 x 0.50 mm. Monoclinic, $P2_1$, *a* = 14.915(1), *b* = 11.853(1), *c* = 7.137(1) Å, β= 93.153(8)°, *V* = 1259.8(2) Å, *Z* = 2, D_x = 1.181 g cm^{-1}, λ(MoK$\bar{\alpha}$) = 0.71073 Å, μ = 1.75 cm , *F*(000) = 488. *Data collection*: The data were collected on an Enraf-Nonius *CAD-4F* diffractometer (Mo tube, 50 kV, 40 mA, monochromated Mo-Kα radiation, Δω = 1.05 + 0.34 tg θ); T = 130 K, range 16.24° < θ < 20.15°, reflections collected: 2541 independent reflections 2371. *Solutions and refinement*: The structure was solved by Patterson methods and extension of the model was accomplished by direct methods applied to difference structure factors using the program *DIRDIF*. Refined anisotropically by full-matrix least squares based on F^2 (SHELXL); data/parameters

2371/448 ; $R(F)$ = 0.0331 [$F_o \geq 4.0\ \sigma(F_o)$], $wR(F^2)$ = 0.0788 [$F^2>0$]; absolute-structure parameters; maximal residual electron density (±0.26(5) e/Å^3). The program PLATON has been used for graphical representations of the crystal structure.

Table 4.2: *Interatomic distances and selected bond angles for compound **2.1e**·HCl*

Interatomic Distances (Å)					
O(1)[a]	-C(7)	1.434(3)[b]	C(17)	-C(18)	1.550(3)
O(2)	-C(18)	1.431(3)	H(31)	-O(1)	0.79(4)
N(1)	-C(1)	1.349(3)	H(32)	-O(2)	0.97(5)
N(1)	-C(5)	1.344(3)	H(33)	-N(1)	0.85(4)
C(1)	-C(17)	1.495(4)	H(31)	-Cl(1)	2.48(4)
C(5)	-C(6)	1.501(3)	H(32)	-Cl(1)	2.33(5)
C(6)	-C(7)	1.554(3)	H(33)	-Cl(1)	2.23(4)

Bond angles (deg.)							
C(1)	-N(1)	-C(5)	124.8(2)	Cl(1)	-H(31)	-O(1)	147(4)
N(1)	-C(1)	-C(17)	117.8(2)	Cl(1)	-H(32)	-O(2)	162(4)
N(1)	-C(5)	-C(6)	118.4(2)	Cl(1)	-H(33)	-N(1)	177(4)
C(5)	-C(6)	-C(7)	116.54(18)	H(31)	-O(1)	-C(7)	109(4)
O(1)	-C(7)	-C(6)	107.32(19)	H(32)	-O(2)	-C(18)	110(3)
C(1)	-C(17)	-C(18)	113.3(3)	H(33)	-N(1)	-C(1)	117(3)
O(2)	-C(18)	-C(17)	107.11(18)	H(33)	-N(1)	-C(5)	118(3)

[a] The numbering for the crystal data does not follow the numbering used in nomenclature.

[b] Standard deviation in parentheses.

2.7b·HCl

This material was prepared in according to the procedure for **2.1e**·HCl starting from **2.7b** (0.55 g, 1.35 mmol). A colorless solid crystallized after addition of hexane (0.53 g, 1.20 mmol, 89%): mp 193-194°C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.06 (s, 2H), 1.24 (m, 2H), 1.4-1.8 (m, 12H), 1.878 (s, 6H), 2.43 (m, 6H), 3.19 (s, 3H), 4.22 (s, 1H), 6.08 (br, 2OH), 7.51 (m, 2H), 8.08 (t, J = 7.81 Hz, 1H); ^{13}C NMR (300 MHz, $CDCl_3$): δ 26.21 (q), 26.74 (d), 32.68 (t), 32.73 (t), 33.96 (t), 34.87 (t), 36.45 (d), 36.57 (d), 37.66 (t), 50.48 (d), 79.45 (s), 125.30 (d), 127.48 (d), 142.76 (d), 154.74 (s), 156.58 (s). HRMS calcd 443.259; no proper HRMS could be obtained; CI(NH_3) gave a molecular ion at m/e 408 (-HCl). Anal. Calcd for $C_{55}H_{78}N_2O_4Cl_4$: C, 67.89; H, 8.08; N, 2.88; Cl 14.57. Found C, 67.21; H, 8.05; N, 2.86; Cl, 14.43.

Crystal Structure 2.7b·HCl

Crystal Data: Formula: $([C_{27}H_{38}NO_2]^+.Cl^-)_2.CH_2Cl_2$, M = 973.05, Suitable colorless crystals were obtained by recrystallization from CH_2Cl_2. The crystal, used for characterization and data collection, was a parallelepiped of approximate size 0.40 x 0.44 x 0.46 mm. The asymmetric units consists of five moieties: two anion complexes, two chlorides anions and one molecule dichloromethane solvent molecule. Monoclinic $P2_1/a$, a = 13.656(4), b = 10.300(1), c = 35.476(5) Å, β = 95.43(2)°, V = 4967.5(17) Å^3, Z = 4, D_x = 1.301 gcm^{-3}, λ(MoK$\bar{\alpha}$) = 0.71073 Å, μ = 2.9 cm^{-1}, F(000) = 2088, T = 130 K. *Data collection*: The data were collected on an Enraf-Nonius *CAD*-4F^2 diffractometer (Mo tube, 50 kV, 40 mA, monochromated Mo-K$\bar{\alpha}$ radiation, Δω = 0.80 + 0.34 tg θ); range 18.16° < θ < 20.52°. Reflections collected: 10746 independent reflections 9688. *Solutions and refinement:* The structure was solved by Patterson methods and extension of the model was accomplished by direct methods applied to difference structure factors using the program *DIRDIF*. Final refinement on F^2 carried out by full-matrix least-squares techniques converged at $wR(F^2)$ = 0.1402 for 9688 reflections with $F_o^2 \geq 0$ and $R(F)$ = 0.0424 for 7896 reflections with $F_o \geq 4.0$ $\sigma(F_o)$ and 898 parameters.

Table 4.3 : *Interatomic distances and selected bond angles for unit 1 of compound **2.7b**·HCl*

Interatomic Distances (Å) of unit 1					
O(1)[a]	-C(8)	1.431(3)[b]	H(102)	-Cl(3)	2.18(3)
O(2)	-C(26)	1.431(3)	H(101)	-O(2)	2.03(4)
O(1)	-H(101)	0.77(4)	H(111)	-N(1)	0.87(3)
O(1)	-H(111)	2.51(3)	C(6)	-C(7)	1.511(3)
O(2)	-H(102)	0.88(3)	C(7)	-C(8)	1.589(3)
Cl(3)	-H(111)	2.36(3)	C(7)	-C(26)	1.590(3)
N(1)	-C(6)	1.356(3)			

Bond angles (deg.) of unit 1							
N(1)	-C(6)	-C(7)	120.87(18)	H(111)	-N(1)	-C(6)	116(2)
C(6)	-C(7)	-C(8)	108.31(17)	C(8)	-O(1)	-H(101)	105(3)
C(6)	-C(7)	-C(26)	115.65(17)	C(26)	-O(2)	-H(102)	109.4(18)
O(1)	-C(8)	-C(7)	108.35(17)	O(2)	-H(102)	-Cl(3)	160(3)
O(2)	-C(26)	-C(7)	109.08(16)	O(1)	-H(101)	-O(2)	141(4)
Cl(3)	-H(111)	-N(1)	158(3)				

[a] The numbering for the crystal data does not follow the numbering used in nomenclature.

[b] Standard deviation in parentheses.

Table 4.4 : *Interatomic distances and selected bond angles for unit 2 of compound **2.7b**·HCl.*

Interatomic Distances (Å) of unit 2					
O(3)[a]	-C(35)	1.439(3)[b]	C(34)	-C(45)	1.589(3)
O(4)	-C(45)	1.436(3)	N(2)	-C(33)	1.355(3)
O(3)	-H(103)	0.81(3)	Cl(4)	-H(112)	2.38(3)
O(4)	-H(104)	0.84(4)	H(112)	-N(2)	0.85(3)
O(3)	-H(104)	1.94(4)	H(112)	-O(4)	2.47(3)
C(33)	-C(34)	1.514(3)	H(103)	-Cl(4)	2.27(3)
C(34)	-C(35)	1.585(3)			

Bond angles (deg.) of unit 2							
N(2)	-C(33)	-C(34)	120.16(19)	C(35)	-O(3)	-H(103)	108(2)
O(3)	-C(35)	-C(34)	108.82(16)	C(35)	-O(3)	-H(104)	106.6(12)
O(4)	-C(45)	-C(34)	108.72(17)	C(45)	-O(4)	-H(104)	106(3)
O(3)	-H(103)	-Cl(4)	166(3)	C(33)	-C(34)	-C(35)	115.71(17)
O(3)	-H(104)	-O(4)	141(4)	C(33)	-C(34)	-C(45)	106.84(17)
Cl(4)	-H(112)	-N(2)	149(3)	N(2)	-H(112)	-O(4)	104(2)
H(112)	-N(2)	-C(33)	120(2)				

[a] The numbering for the crystal data does not follow the numbering used in nomenclature.

[b] Standard deviation in parentheses.

2.1b·HBr

The adamantanone adduct **2.1b** (0.25 g, 0.61 mmol) was dissolved in 10 mL of chloroform and HBr was slowly passed through the solution for 5 min at 0°C. After removal of the solvent the product was recrystallized twice from ethanol yielding a colorless solid (44%, 0.13 g, 0.27 mmol): mp > 240°C; IR (KBr): 3370, 2905, 1635, 1625, 1070, 1025, 925, 820, 760; ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.4-2.1 (m, 24H), 2.26 (d, *J* = 12.94 Hz, 4H), 3.67 (s, 4H), 3.84 (s, 2H), 7.37 (d, *J* = 7.81 Hz, 2H), 8.09 (t, *J* = 7.81 Hz, 1H); ^{13}C NMR (500 MHz, $CDCl_3$): δ 27.16 (d), 27.37 (d), 32.72 (t), 34.44 (t), 37.07 (d), 38.24 (t), 40.65 (t), 75.59 (s), 125.05 (d), 142.72 (d), 154.45 (s); HRMS calcd 487.209; found 407.282 (-HBr). Anal. Calcd for $C_{27}H_{38}NO_2Br$: C, 66.39; H, 7.84; N, 2.87, Br 16.36. Found C, 66.27; H, 7.80; N, 2.87, Br 16.36.

3.11f·HBr

This product was prepared according to the method described for **2.1b**·HCl starting from **3.11f** (0.75 g, 2.7 mmol). After HBr addition was stopped hexane was added and the complexes precipitated from the solution. the product was recrystallized from chloroform/hexane affording colorless needles (0.92 g, 2.6 mmol, 95%). mp 217-218 °C; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 0.87 (s, 3H), 1.05 (s, 3H), 1.14 (s, 3H), 1.18 (m, 1H), 1.34 (d, *J* = 11.7 Hz, 1H), 1.40 (m, 1H),

1.56 (s, SH), 1.61 (m, 1H), 1.66 (m, 1H), 2.27 (d, *J* = 11.0 Hz, 1H), 2.38 (m, 1H), 2.99 (s, 3H), 3.26 (d, *J* = 17.2 Hz, 1H), 4.47 (d, *J* = 17.2 Hz, 1H), 7.44 (d, *J* = 7.69 Hz, 1H), 8.11 (dd, *J* = 8.05 Hz, *J* = 7.69 Hz, 1H), 8.79 (d, *J* = 8.05 Hz, 1H); ^{13}C-NMR (300 MHz, $CDCl_3$) δ 17.68 (q), 19.16 (q), 24.41 (t), 26.04 (q), 29.42 (q), 33.77 (t), 40.23 (t), 44.28 (t), 45.37 (s), 50.70 (d), 56.21 (s), 63.29 (s), 124.69 (d), 125.17 (d), 143.43 (d), 153.54 (s), 157.82 (s); HRMS calcd. 355.097, found 275.171 (-HBr). Anal. Calcd. for $C_{17}H_{26}NSBr$: C, 57.30; H, 7.35; N, 3.93; S, 9.00. Found C, 57.36; H, 7.37; N, 3.94, S; 8.98.

3.1b·HBr

This product was prepared analogously to **2.1b**·HBr starting from a solution of dithiol **3.1b** 0.10 g, 0.23 mmol) in 10 mL of $CHCl_3$ at 0°C. Evaporation of the solvent at reduced pressure yielded the crude HBr complex as a white powder, which was crystallized from $CHCl_3$/hexane to afford **3.1b**·HBr as colorless needles (0.09 g, 0.17 mmol, 75%): mp > 220 °C; ^{1}H NMR ($CDCl_3$): δ 1.8 (m, 20H), 2.27 (d, J=12.9 Hz, 4H), 2.52 (d, J=11.7 Hz), 4H), 3.27 (s, SH), 4.09 (s, 4H), 7.45 (d, *J* = 8.1 Hz, 2H), 8.15 (dd, *J* = 8.1 Hz, 1H); ^{13}C NMR ($CDC1_3$): δ 27.79 (CH), 28.21 (CH), 33.99 (CH_2), 34.38 (CH_2), 38.54 (CH), 39.78 (CH_2), 42.84 (CH_2), 57.08 (C), 99.88 (C), 125.77 (CH), 143.64 (CH), 155.94 (C); HRMS calcd for $C_{27}H_{38}NS_2$ Br 519.163, found 439.237 (-HBr).

2.1b·HNO3

The diol adduct **2.1b** (0.20 g, 0.49 mmol) was dissolved in 10 mL of chloroform and cooled to 0°C. HNO_3 100% (32 mg, 0.5 mmol) was added and stirring was continued for 30 min. After removal of the solvent the product was recrystallized from methanol yielding a white solid (95%, 0.22 g, 0.47 mmol): mp 194-196°C; IR (KBr): 3385, 2905, 1635, 1450, 1321, 1200, 1070, 1025, 930, 825, 760; ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.52 (d, *J* = 13.19 Hz, 4H), 1.71 (s, 8H), 1.87 (m, 12H), 2.13 (d, *J* = 10.5 Hz, 4H), 3.42 (s, 4H), 7.42 (d, *J* = 7.82 Hz, 2H), 8.12 (t, *J* = 7.82 Hz, 1H); ^{13}C NMR (200 MHz, $CDCl_3$): δ 26.93 (d), 27.17 (d), 32.56 (t), 34.34 (t), 36.77 (d), 38.03 (t), 41.83 (t), 75.37 (s), 125.01 (d), 143.01 (d), 154.48 (s). HRMS calcd. 470.278; found 407.282 (-HNO_3). Anal. Calcd for $C_{27}H_{38}N_2O_5$: C, 68.91; H, 8.14; N, 5.95. Found C, 68.64; H, 8.11; N, 6.01.

3.1b·HNO_3

This product was prepared according to the method used for the preparation of **2.1d**·HNO_3, at 0°C starting from dithiol **3.1b** (0.45 g, 1.03 mmol). The product was recrystallized from $CHCl_3$/hexane by slow evaporation of the solvent (mainly chloroform) to obtain **3.1b**·HNO_3 as colorless crystals (0.34 g., 0.69 mmol, 67%). ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.8-2.2 (m, 20H), 2.40 (d, *J* = 11.7 Hz, 2H), 2.65 (d, *J* = 11.7 Hz, 2H), 3.94 (s, 4H), 7.65 (d, *J* = 7.7 Hz, 2H), 8.24 (t, *J* = 7.7 Hz, 1H).

Crystal Structure of HNO_3 complex of 3.1b

Crystal Data: *Formula*: $[C_{27}H_{38}NS_2]^+.[NO_3]^-$, M = 502.74, Suitable colorless thin plate-shaped crystals of approximate size 0.02 x 0.23 x 0.32 mm were obtained by recrystallization from chloroform/hexane. monoclinic, *Pc*, *a* = 6.824(2), *b* = 16.118(4), *c* = 11.972(4) Å, , β = 102.68(3)°, *V* = 1284.7(7) Å, *Z* = 2, D_x = 1.300 g cm^{-1}, λ(MoK$\bar{\alpha}$) = 0.71073 Å, μ = 2.4 cm , *F*(000) = 540; T = 130 K. The asymmetric unit consists of two moieties: a cation complex and as counter anion NO_3^-. *Data collection:* The data were collected on an Enraf-Nonius *CAD-4F*^{2} diffractometer (Mo tube, 50 kV, 40 mA, monochromated Mo-K$\bar{\alpha}$ radiation, Δω = 1.05 + 0.34 tg θ), range 8.35° < θ < 18.41°, reflections collected: 5373 independent reflections: 2542. *Solutions and refinement*: The structure was solved by Patterson methods and extension of the model was accomplished by direct methods applied to difference structure factors using the program *DIRDIF*. Final refinement converged at *wR*(F^2) = 0.0883 for 2542 reflections with $F_o^2 \geq 0$ and 342 parameters and *R*(*F*) = 0.0457 for 1862 reflections with $F_o \geq 4.0\ \sigma(F_o)$.

Table 4.5*: Interatomic distances and selected bond angles for compound* ***3.1b·****HNO_3.*

Interatomic Distances (Å)					
S(1)[a]	-C(7)	1.838(5)[b]	S(2)	-H(32)	1.43(6)
S(2)	-C(18)	1.861(6)	S(1)	-H(31)	1.24(5)
N(1)	-C(1)	1.344(7)	O(1)	-N(2)	1.241(6)
N(1)	-C(5)	1.341(7)	O(2)	-N(2)	1.259(6)
N(1)	-H(33)	0.87(5)	O(3)	-N(2)	1.244(7)
C(1)	-C(17)	1.508(7)	H(33)	-O(2)	1.92(5)
C(5)	-C(6)	1.502(7)	H(33)	-O(3)	2.58(5)
C(6)	-C(7)	1.550(7)	H(32)	-O(2)	2.26(5)
C(17)	-C(18)	1.558(7)	H(31)	-O(3)	2.21(5)

Bond angles (deg.)							
C(1)	-N(1)	-C(5)	124.8(5)	O(1)	-N(2)	-O(3)	121.2(4)
N(1)	-C(1)	-C(17)	116.8(5)	O(1)	-N(2)	-O(2)	120.6(4)
N(1)	-C(5)	-C(6)	117.2(5)	O(2)	-N(2)	-O(3)	118.2(4)
C(5)	-C(6)	-C(7)	115.3(4)	O(2)	-H(33)	-N(1)	162(5)
S(1)	-C(7)	-C(6)	108.3(3)	O(3)	-H(33)	-N(1)	143(4)
C(1)	-C(17)	-C(18)	115.8(5)	C(18)	-S(2)	-H(32)	92(2)
S(2)	-C(18)	-C(17)	107.9(3)	C(7)	-S(1)	-H(31)	92(2)
C(1)	-N(1)	-H(33)	117(3)	S(2)	-H(32)	-O(2)	156(3)
C(5)	-N(1)	-H(33)	118(3)	S(1)	-H(31)	-O(3)	160(3)

[a] The numbering for the crystal data does not follow the numbering used in nomenclature.

[b] Standard deviation in parentheses.

General procedure for ring opening of cyclohexene oxides 4.1a and 4.1b.

To a stirred solution of epoxide **4.1** (0.25 mmol) in 5 mL of CH_2Cl_2 was added the hydrogen chloride or hydrogen bromide complex (0.25 mmol) stirring continued for 3h in which the reaction ran to completion. The solution was filtered and the e.e. and conversion were measured by means of chiral GC (Chiradex BTA (astec) 50m x 0.25 mm x 0.25 μm).

trans-2-chlorocyclohexanol 4.2a

^{1}H-NMR (300 MHz, $CDCl_3$) δ 1.31 (m, 3H), 1.72 (m, 3H), 2.10 (m, 2H), 2.59 (s, OH), 3.48 (m, 1H), 3.73 (m, 1H); ^{13}C-NMR (300 MHz, $CDCl_3$) δ 23.66 (t), 25.32 (t), 32.87 (t), 34.87 (t), 67.16 (d), 77.53 (d).

trans-2-chlorocyclopentanol 4.2b

^{1}H-NMR (300 MHz, $CDCl_3$) δ 1.59 (m, 1H), 1.84 (m, 3H), 2.10 (s, OH), 2.14 (m, 2H), 2.25 (m, 1H), 4.00 (m, 1H), 4.24 (m, 1H); ^{13}C-NMR (300 MHz, $CDCl_3$) δ 20.10 (t), 30.87 (t), 32.85 (t), 65.33 (d), 79.91 (d).

trans-2-bromocyclohexanol 4.3a

^{1}H-NMR (300 MHz, $CDCl_3$) δ 1.30 (m, 3H), 1.67 (m, 1H), 1.79 (m, 2H), 2.11 (m, 1H), 2.30 (m, 1H), 2.46 (s, OH), 3.58 (m, 1H), 3.87 (m, 1H); ^{13}C-NMR (300 MHz, $CDCl_3$) δ 24.03 (t), 26.59 (t), 33.43 (t), 36.12 (t), 61.76 (d), 77.38 (d).

trans-2-bromocyclopentanol 4.3b

^{1}H-NMR (300 MHz, $CDCl_3$) δ 1.55 (m, 1H), 1.78 (m, 2H), 1.96 (m, 1H), 2.13 (m, 1H), 2.31 (m, 1H), 2.93 (s, OH), 4.00 (m, 1H), 4.29 (m, 1H); ^{13}C-NMR (300 MHz, $CDCl_3$) δ 19.84 (t), 30.92 (t), 33.63 (t), 56.82 (d), 80.18 (d).

Complexation of $Zn(NO_3)_2$ with 2.1b

To a stirred solution of **2.1b** (0.10 g, 0.25 mmol) in chloroform (2 mL) was added a solution of $Zn(NO_3)_2.6H_2O$ (74 mg, 0.25 mmol) in methanol (1 mL). The mixture was stirred overnight and concentrated. The solid was washed with dichloromethane and recrystallized from ethyl acetate/methanol by evaporation of the methanol (0.11 g, 0.19 mmol, 78%): ^{1}H NMR (300 MHz, CD_3OD): δ 1.38 (m, 4H), 1.50 (s, 4H), 1.62 (m, 10H), 1.76 (s, 2H), 2.11 (m, 4H), 2.27 (m, 4H), 3.14 (s, 4H), 7.07 (d, *J* = 7.69 Hz, 2H), 7.50 (t, *J* = 7.69 Hz, 1H); Anal. Calcd for $C_{27}H_{37}N_3O_8Zn$: C, 54.32; H, 6.25; N, 7.04. Found C, 54.31; H, 6.27; N, 7.04.

Complexation of $Zn(NO_3)_2$ with 2.1d

This material was prepared according to the procedure reported above for the complexation of **2.1b** starting from **2.1d** (70 mg, 0.17 mmol) and $Zn(NO_3)_2.6H_2O$ (50 mg, 0.17 mmol) After stirring overnight in a mixture of chloroform/methanol (1:1) the solvent was removed and the solid was washed with hexane. After recrystallization form chloroform/hexane the product was obtained as colorless crystals in which methanol is embedded (93 mg, 0.15 mmol, 91%): mp 168-170°C; $[\alpha]^{23}_D$ –5.0 (*c* 0.6, acetone); ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.82 (s,6H), 0.92 (s, 6H), 1.00 (s, 6H), 1.08 (m, 2H), 1.43 (m, 6H), 1.74 (m, 6H), 2.99 (d, *J* = 13.18 Hz, 2H), 3.30 (d, *J* = 13.18 Hz, 2H), 7.52 (d, *J* = 8.06 Hz, 2H), 8.09 (t, *J* = 8.06 Hz, 1H); ^{13}C NMR (300 MHz, $CDCl_3$): δ 10.66 (q), 21.06 (q), 21.14 (q), 27.20 (t), 30.63 (t), 41.27 (t), 43.31 (t), 44.92 (d), 49.01 (s), 53.59 (s), 80.91 (s), 125.47 (d), 142.67 (d), 155.15 (s). Anal. Calcd for $C_{27}H_{41}N_3O_8Zn$: C, 53.12; H, 7.16; N, 6.64; Zn, 10.33. Found C, 52.64; H, 7.23; N, 6.56; Zn, 10.25.

Complexation of $Zn(NO_3)_2$ with 2.7b

To a stirred solution of **2.7b** (0.25 g, 0.61 mmol) in 3 mL of chloroform was added $Zn(NO_3)_2.6H_2O$ (0.18 g, 0.61 mmol) and the mixture was stirred overnight. The formed solid was washed with chloroform and recrystallized from methanol/ethyl acetate by slow evaporation of the methanol affording the complex as colorless crystals (0.30 g, 0.51 mmol, 84%): ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.67 (s, 2H), 1.25 (m, 2H), 1.40 (m, 2H), 1.52 (m, 2H), 1.61 (m, 6H), 1.79 (m, 6H), 2.05 (m, 4H), 2.26 (m, 2H), 2.35 (m, 2H), 2.75 (s, 3H), 4.25 (s, 1H), 7.68 (d, *J* = 7.69 Hz, 1H), 7.95 (d, *J* = 7.69 Hz, 1H), 8.22 (dd, *J* = 7.69 Hz, *J* = 7.69 Hz, 1H); Anal. Calcd for $C_{27}H_{37}N_3O_8Zn$ C, 54.44; H, 6.27; N, 7.06. Found C, 54.24; H, 6.21; N, 7.01.

4.4b

The dithiol **3.1b** (0.12 g, 0.27 mmol) was dissolved in 5 mL of chloroform and a solution of $Zn(NO_3)_2.6H_2O$ (0.08 g, 0.27 mmol) in 5 ml of methanol was added the mixture was stirred overnight and filtered yielding the dimeric zinc complex **4.4b** (0.10 g, 0.21 mmol, 75%). ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.4-1.8 (m, 20H), 1.92 (m, 1H), 2.18 (m, 1H), 2.36 (m, 2H), 2.59 (m, 2H), 3.05 (m, 1H), 3.12 (d, J = 14.3 Hz, 1H), 3.38 (d, J = 15.4 Hz, 1H), 4.01 (d, J = 15.4 Hz, 1H), 4.10 (d, J = 14.3 Hz, 1H), 7.29 (m 2H), 7.68 (m, 1H); Anal. Calcd for $C_{27}H_{35}NS_2Zn$ C, 64.65; H, 7.04; N, 2.79; Zn, 12.76. Found C, 64.34; H, 7.15; N, 2.75.

4.6

The dithiol **3.1b** (0.25 g, 0.57 mmol) was suspended in 5 mL of methanol and a solution of $ZnCl_2$ (76 mg, 0.57 mmol) in 5 mL of methanol was added. Stirring remained overnight and the mixture was subsequently filtered yielding the dimeric complex **4.4b** (80 mg, 0.16 mmol, 28%).

The solvent from the mother liquor was evaporated under high vacuum. Ethanol was added to obtain a soluble product in chloroform which was recrystallized from chloroform/hexane affording the complex **4.6** as colorless crystals (0.21 g, 0.29 mmol, 60%): ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.27 (t, J = 7.1 Hz, EtOH), 1.6-2.0 (m, 20H), 2.26 (d, J = 12.0 Hz, 4H), 2.47 (d, J = 12.0 Hz, 4H), 3.52 (s, MeOH), 3.84 (s, 4H), 3.89 (q, J = 7.1 Hz, EtOH), 7.69 (d, J = 7.8 Hz, 2H), 8.28 (t, J = 7.8 Hz, 1H).

Crystal Structure of 4.6

*Crystal Data: Formula***:** $[C_{27}H_{38}NS_2]^+[ZnCl_3X]^-.CHCl_3$, where X = CH_2OH or C_2H_5OH, M = 770.08. Suitable transparent block-shaped crystals were obtained by recrystallization from chloroform. The crystal, a parallelepiped of approximate size 0.20 x 0.22 x 0.44 mm was used for data collection. The asymmetric unit consists of three moieties: a cationic ligand, a anionic Zn-complex and a chloroform solvent molecule. In the anionic Zn-complex the coordinated alcohol is a mixture of methanol / ethanol (56:44). The crystal was triclinic, $P\bar{}$, a = 10.622(2), b = 11.641(1), c = 15.032(1) Å, α = 87.359(9)°, β = 71.31(1)°, γ = 78.74(1)°, V = 1726.5(4) Å, Z = 2, D_x = 1.481 g cm^{-1}, λ(MoK$\bar{\alpha}$) = 0.71073 Å, μ = 13.2 cm^{-1}, F(000) = 799, T = 130 K. *Data collection*: The data were collected on an Enraf-Nonius *CAD*-4F^2 diffractometer (Mo tube, 50 kV, 40 mA, monochromated Mo-K$\bar{\alpha}$ radiation, Δω = 0.85 + 0.34 tg θ), range 17.85° < θ < 20.17°. Reflections collected: 7928 independent reflections: 7306. *Solutions and refinement*: The structure was solved by Patterson methods and extension of the model was accomplished by direct methods applied to difference structure factors using the program *DIRDIF*. $wR(F^2)$ = 0.0961 for 7306 reflections with $F_o^2 \geq 0$ and 532 parameters and $R(F)$ = 0.0364 for 6691 reflections obeying $F_o \geq 4.0\ \sigma(F_o)$ criterion of observability.

Table 4.6*: Interatomic distances and selected bond angles of* ***4.6*** **.**

Interatomic Distances (Å)					
S(1)[a]	-C(7)	1.840(2)[b]	Zn	-O(1)	2.018(2)
S(2)	-C(18)	1.845(2)	O(1)	-C(28)	1.399(4)
N(1)	-C(1)	1.351(3)	C(28)	-C(29)	1.492(8)
N(1)	-C(5)	1.347(3)	H(31)	-S(1)	1.21(4)
C(1)	-C(17)	1.495(3)	H(32)	-S(2)	1.26(3)
C(5)	-C(6)	1.494(3)	H(33)	-N(1)	0.87(3)
C(6)	-C(7)	1.559(3)	H(33)	-Cl(2)	2.35(3)
C(17)	-C(18)	1.556(3)	H(32)	-Cl(2)	2.73(3)
Zn	-Cl(1)	2.2114(9)	H(34)	-O(1)	0.74(3)
Zn	-Cl(2)	2.2425(8)	H(34)	-Cl(3)	2.32(3)
Zn	-Cl(3)	2.2536(8)	H(31)	-Cl(1)	2.909

Bond angles (deg.)							
C(1)	-N(1)	-C(5)	125.21(18)	Cl(3)	-Zn	-O(1)	108.08(6)
C(5)	-C(6)	-C(7)	114.26(17)	S(1)	-C(7)	-C(6)	107.28(14)
C(1)	-C(17)	-C(18)	115.38(18)	S(2)	-C(18)	-C(17)	107.63(14)
C(5)	-N(1)	-H(33)	117(2)	N(1)	-H(33)	-Cl(2)	167(3)
C(1)	-N(1)	-H(33)	118(2)	N(1)	-C(1)	-C(17)	117.65(18)
C(28)	-O(1)	-H(34)	107(2)	N(1)	-C(5)	-C(6)	117.84(18)
Cl(2)	-Zn	-O(1)	101.94(6)	H(31)	-S(1)	-C(7)	93(2)
Cl(1)	-Zn	-Cl(2)	116.43(3)	H(32)	-S(2)	-C(18)	95(3)
Cl(1)	-Zn	-Cl(3)	115.17(3)	Zn	-O(1)	-C(28)	124.89(18)
Cl(1)	-Zn	-O(1)	102.45(6)	Zn	-O(1)	-H(34)	122(2)
Cl(2)	-Zn	-Cl(3)	111.10(3)				

[a] The numbering for the crystal data does not follow the numbering used in nomenclature.

[b] Standard deviation in parentheses.

4.5f

To a solution of dithiol **3.1f** (0.25 g, 0.56 mmol) in 5 mL of chloroform was added $Zn(NO_3)_2.6H_2O$ (0.17 g, mmol) in 5 mL of methanol. The mixture was stirred overnight filtered and concentrated in vacuo yielding the complex **4.4f** as a white solid (0.17 g, 0.34 mmol, 60%): ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.68 (s, 6H), 1.2-1.8 (m, 22H), 1.96 (d, J = 10.4 Hz, 2H), 2.64 (m, 2H), 3.49 (m, 2H), 3.66 (m, 2H), 7.17 (d, J = 7.7 Hz, 2H), 7.61 (t, J = 7.7 Hz, 1H). HRMS calcd 505.182, found 505.183. Anal. Calcd for $C_{27}H_{39}NS_2Zn$: C, 63.95; H, 7.75; N, 2.76. Found C, 63.65; H, 7.65; N, 2.86 .

Complexation of 3.1f with $Co(NO_3)_2$

To a solution of dithiol **3.1f** (0.22 g, 0.50 mmol) in 5 mL of chloroform was added $Co(NO_3)_2.6H_2O$ (0.15 g, 0.50 mmol). After stirring for 1.5 h the mixture was stored at –20 °C overnight. A purple solid was formed and filtered affording the dimeric complex (0.09 g, 0.18 mmol, 35%): ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.43 (s, 3H), 0.60 (s, 3H), 1.1-1.4 (m, 16H), 1.7 (m, 8H), 1.98 (m, 1H), 2.44 (m, 1H), 2.82 (d, J = 15.3 Hz, 1H), 2.98 (d, J = 14.1 Hz, 1H), 3.27 (d, J = 14.1 Hz, 1H), 3.35 (d, J = 15.3 Hz, 1H), 6.65 (d, J = 7.7 Hz, 1H), 7.28 (m, 1H), 7.93 (d, J = 7.7 Hz, 1H), 7.61 (t, J = 7.7 Hz, 1H). Anal. Calcd for $C_{27}H_{39}NS_2Co$: C, 64.77; H, 7.85; N, 2.80. Found C, 64.55; H, 7.74; N, 2.90.

4.8 References.

* Koning, B.; Hulst, R.; Bouter, A.; Buter, J.; Meetsma, A.; Kellogg, R.M. *Chem. Commun.* **1997**, 1065.

1 Edema, J.J.; Libbers, R.; Ridder, A.M.; Kellogg, R.M.; van Bolhuis, F.; Kooijman, H.; Spek, A.L. *J. Chem. Soc., Chem. Commun*. **1993**, 625.

2. Zeng, Y.P.; Sharpe, S.W.; Reifschneider, D.; Wittig, C.; Beandet, R.A. *J. Chem. Phys.* **1990**, *93*, 183.

3 Truscott, C.E.; Ault, B.S. *J. Phys. Chem.* **1984**, *88*, 2323.

4. Greenwood, N.N.; Earnshaw, A. in *Chemistry of the Elements*, Pergamon Press, New York, **1984**, p. 949.

5 Edema, J.J.; Libbers, R.; Ridder, A.M.; Kellogg, R.M.; Spek, A.L. *J. Organomet. Chem.* **1994**, 127.

6 The enantiomeric excess was determined by means of chiral GC on a Chiradex BTA (astec) 50m x 0.25 mm x 0.25 μm.

7 Kaptein, B.; Barf, G.; Kellogg, R.M.; Van Bolhuis, F. *J. Org. Chem*. **1990**, *55*, 1890.

8 Mack, H.; Eisen, M.S. *J. Chem. Soc., Dalton Trans* **1998**, 917.

9 Berg, J. M.; Holm, R. H. *J. Am. Chem. Soc*. **1984**, *106*, 3035.

10 Li, Z-Y.; Yu, W-Y.; Che, C-M.; Poon, C-K.; Wang, R-J.; Mak, T.C.W. *J. Chem. Soc., Dalton Trans* **1992**, 1657.

11 Igai, S.; Imaoka, I; Mitani, N.; Ube Industries, Japan; patent JP 09012582 A2, **1997** CA 126:225669.

12 Chan, P-M.; Yu, W-Y.; Che, C-M.; Cheung, K-K. *J. Chem. Soc., Dalton Trans* **1998**, 3183.

13 Spek, A.L. (**1993**). *HELENA. Program for Reduction of CAD*4 *Data*. Utrecht Univ. The Netherlands.